REMARKS

FORMAL MATTERS:

Claims 77-101 are pending and stand rejected.

Claims 1-76 and 102-106 are cancelled.

In view of the remarks set forth below, reconsideration of this application is respectfully requested.

REJECTION UNDER §101

Claims 77-101 stand rejected under 35 U.S.C. § 101 as lacking patentable utility. The Applicants respectfully traverse this rejection.

In summary, the instant specification shows that the GPCR hARE-2 is selectively expressed in an area of the brain - the *substantia nigra* – that degenerates in Parkinson's disease. The specific degeneration of these cells results in Parkinson's disease.

As will be described in greater detail below, the observation that hARE-2 is selectively expressed in the same cells that die in Parkinson's disease provides at least *two* utilities for the claimed subject matter.

The selective expression pattern of hARE-2 in *substantia nigra* cells allows for modulation of the intracellular levels of downstream signaling molecules (cAMP, IP_3 and/or Ca^{2+}) *selectively* in those cells. Fluctuations in the intracellular levels of these very same molecules are correlated with the viability of *substantia nigra* cells[1]. Thus, hARE-2 can be used to identify compounds that modulate the intracellular levels of molecules that are directly implicated in the survival of those cells. Stated differently, screening methods to identify compounds that modulate hARE-2's effect upon intracellular cAMP, IP_3 and/or Ca^{2+} facilitates identification of compounds that increase the "well-being" of *substantia nigra* cells and stave off or slow the progression of Parkinson's disease.

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[1] *See, e.g.*, Hulley et al, Inhibitors of type IV phosphodiesterases reduce the toxicity of MPTP in *substantia nigra* neurons *in vivo*. Eur. J. Neurosci. 1995 Dec 1;7(12):2431-40; and Hirsch et al, Neuronal vulnerability in Parkinson's disease. J Neural Transm Suppl. 1997;50:79-88, as discussed in prior response.

This first utility relies on well established links, namely: a) that GPCRs modulate the levels of intracellular signaling molecules and b) that the same GPCR-modulated intracellular signaling molecules affect the "well being" of *substantia nigra* cells (see, e.g., the references in footnote 2, below).

A review of the Office Action indicates that the Examiner appears to understand the logic used to support this utility. That said, the Examiner still disagrees that the claimed subject matter meets the requirement of 35 U.S.C. § 101.

The Applicants also submit that the claimed subject matter can be employed to identify compounds that facilitate detection of hARE-2-expressing cells, and thus can facilitate diagnosis and/or monitoring of Parkinson's disease. For example, a compound identified by using the claimed composition may be used in radio-imaging methods for the study of Parkinson's disease, in a similar manner to the compounds as described in Leenders et al. (Arch. Neurol 1990 47:1290-1298) and Fischman et al. (Synapse 1998 29:128-141). This additional utility also exploits the selective expression of hARE-2 in *substantia nigra* cells.

With respect to this second utility, the Applicants submit that hARE-2 is conceptually no different from a marker of other cell types that degenerate during the manifestation of a disease. For example, the Applicants submit that hARE-2 is conceptually no different from a marker for islet cells, which are known to degenerate to result in insulin disorders such as type II diabetes. Likewise, using the same logic, detection of hARE-2 as a marker of *substantia nigra* cells is conceptually no different from, for example, a marker for oligodendrocytes (the degeneration of which cause nerve demyelination and multiple sclerosis), or a marker for cells of the macula (which die during macular degeneration to cause blindness).

The Applicants submit that each of the above-described utilities for hARE-2 encoding polynucleotides is credible, specific and substantial. Since no more is required to meet the requirements of 35 U.S.C. §101, the Applicants submit that this rejection should be withdrawn.

In this Office Action, the Examiner argues that the claimed subject has no patentable utility because: a) hARE-2 has not been linked to a particular secondary messenger; b) it is unclear whether inhibition of hARE-2 is good or bad for *substantia nigra* cells; c) there is no apparent correlation between hARE-2 and any particular disease; d) the function and ligand for

hARE-2 are unknown; and e) citing *Brenner v. Manson*[2], the Examiner believes that more research needs to be performed on the claimed subject matter before it can become patentable.

While the Applicants fully understand the Examiner's arguments, the Applicants submit that none of the arguments, individually or in combination, undermine the Applicant's position in any way.

For example, with respect to argument a), i.e., that hARE-2 lacks utility because it has not been linked to a particular secondary messenger, the Applicants submit that *all* GPCRs can modulate either Ca^{2+} (*via* IP_3) or cAMP. Since *either* of these molecules can effect the well-being *substantia nigra* cells (see the *Hulley* and *Hirsch* references cited in the footnote on page 2 of this response and discussed in the prior response), knowledge of the particular secondary messenger system used by hARE-2 has no bearing on whether or not hARE-2 encoded by the claims polynucleotides has a utility in satisfaction of the requirement of §101.

With respect to argument b), i.e., that hARE-2 lacks utility because it is unclear whether inhibition of hARE-2 is good or bad for *substantia nigra* cells, the Applicants submit that the rejected claims neither require a hARE-2 inhibitor nor require inhibition of hARE-2 activity. Thus, the rejected claims are *not* limited to a composition that is only useful for inhibition of hARE-2.

In making this argument, the Examiner appears to be reading limitations into the claims that are not expressly recited. Since, according to MPEP § 2111, it is impermissible to read limitations in to the claims that are not expressly recited, this argument lacks force.

With respect to argument c), i.e., that hARE-2 lacks utility because no apparent correlation with a disease exists, the Applicants submit that a correlation between hARE-2 and Parkinson's disease clearly exists because hARE-2 is selectively expressed in the very cells that degenerate to cause Parkinson's disease. In making this argument, the Examiner appears to be requiring either an up- or down-regulation of hARE-2 in Parkinson's diseased cells. The Applicants note, however, that *substantia nigra* cells *die* during Parkinson's disease. As such, the Applicants believe that the Examiner's requirement for hARE-2 to altered expression in Parkinson's diseased cells is overly stringent. While the expression pattern of hARE-2 by itself

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[2] *Brenner v. Manson* 148 U.S.P.Q. 689 (Supreme Court 1966)

does not demonstrate that hARE-2 is directly involved in the development of the Parkinson's phenotype, a clear correlation nevertheless exists.

With respect to argument d), i.e., that hARE-2 lacks utility because the function and/or ligand for hARE-2 is unknown, the Applicants submit that the *substantia nigra*-selective expression of hARE-2 makes hARE-2 conceptually no different from any marker for a diseased cell that, by virtue of its selective expression, is targeted in the treatment or diagnosis of the disease without any knowledge of the actual function of the marker nor knowledge of the ligand to which the marker binds. For example, the marker HER2 can be employed to deliver drugs to breast cancer cells without any knowledge of the actual function of HER2 nor knowledge of the ligand to which HER2 binds. The utilities described above require no knowledge of the ligand or the function of the hARE-2, and, as such, this argument does not undermine the Applicants' position.

Finally, with respect to argument e), i.e., that hARE-2 lacks utility because more research needs to be performed, the Applicants submit that the expression pattern of hARE-2, combined with knowledge that hARE-2 is a GPCR capable of modulating intracellular levels of cAMP, IP_3 and/or Ca^{2+}, provides a clear path towards hARE-2 as a target for treatment of Parkinson's disease.

In addition, the Applicants note that the facts of this case are completely different to the facts presented in *Brenner v. Manson,* in which the claims were directed to a process for making chemical compounds for which no activity (and thus no use) had been substantiated. This is very different from the situation here because the *substantia nigra*-selective expression pattern of hARE-2 provides a very clear path to Parkinson's disease.

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is respectfully requested.

If this rejection is maintained, the Examiner is requested to explain in more detail the rationale behind the Examiner's assertion that the utility asserted in the prior response – the use of the claimed method to identify compounds for treating Parkinson's disease and other diseases caused by degeneration of the *substantia nigra* – is thought to be neither specific nor substantial, as indicated in ¶5 on page 2 of the Office Action. To be specific, the Applicant's cannot see the

conceptual difference between Parkinson's disease and other diseases, e.g., breast cancer or HIV, that renders Parkinson's disease non-specific and insubstantial. Clarification is requested.

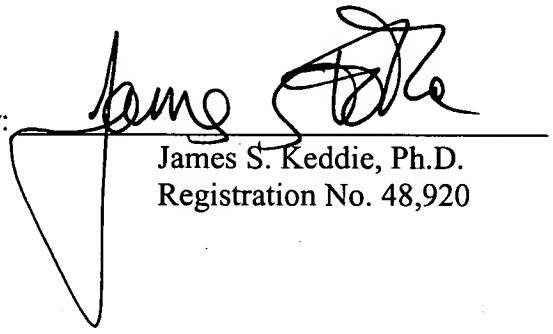
CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number AREN-011DIV.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 19, 2007

By: 
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